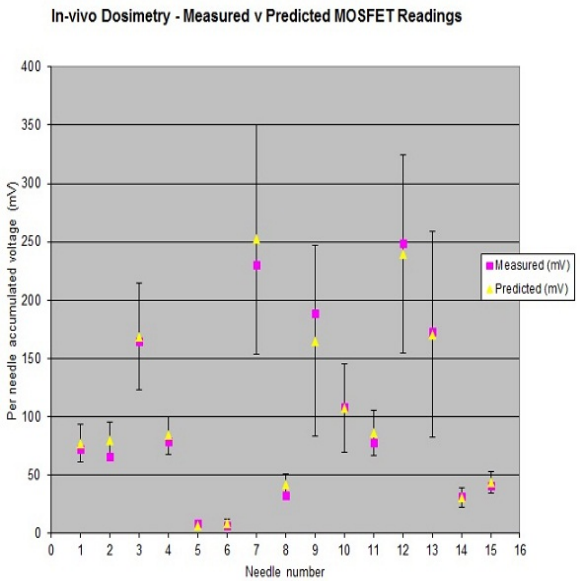
Material and Methods: In vivo dosimetry was performed for 40 HDR prostate brachytherapy patients treated with single fractions of 15Gy (boost) or 19Gy (monotherapy). Treatments were planned using intra-operative trans-rectal ultrasound (TRUS) and for in-vivo dosimetry, an additional needle was inserted centrally in the prostate gland and dose measured using a MOSFET. MOSFET measurements were compared to predicted readings based on exported treatment planning system (TPS) data, per-needle and for total plan dose. To assess impact of needle movement between planning TRUS and treatment, TRUS images were acquired immediately after treatment for 20 patients. To assess impact of heterogeneities (for example steel needles) on the dose at the MOSFET position Monte Carlo (MC) simulations of treatment plans were performed for 10 patients. A retrospective investigation of thresholds for real-time error detection was based on per-needle and total plan uncertainty analysis. Uncertainties included MOSFET calibration/commissioning results, source calibration, TPS, relative source/ MOSFET position and MOSFET reading reproducibility.

Results: The mean measured total plan reading was 6.6% lower than predicted (range +5.1% to -15.2%). Plan reconstruction on post-treatment TRUS showed mean reduction in dose at the MOSFET position of 1.8% due to needle movement. MC simulations showed that heterogeneities caused a mean dose reduction at the MOSFET position of 1.6%. Uncertainty estimates varied between individual treatment plans, for example the uncertainty is higher if the MOSFET is close to a heavily weighted source position. Assuming a source/MOSFET position uncertainty of 1mm, total plan dose uncertainty (k=2) ranged from 10.6% to 17.0% and per needle dose uncertainty (k=2) ranged from 18.2% to 110% (mean 31.0%). Retrospectively applying these uncertainty estimates as error detection thresholds resulted in 1 out of 40 plans and 5% of needles being outside the error detection threshold. The figure shows an example for one patient of predicted versus measured reading for each needle with the k=2 uncertainty illustrated by error bars.



Conclusion: In vivo measurements of dose during HDR prostate brachytherapy treatment delivery show good agreement with TPS predictions within measurement uncertainties, providing reassurance in the accuracy of dose delivery. Thresholds for real-time in vivo error detection using this measurement technique should be calculated on an individual plan basis but would still be likely to generate some false errors, with the main limitation of the measurement technique being that dose is only measured at a single point.

OC-0064

A prediction model for biochemical failure after salvage Iodine-125 prostate brachytherapy

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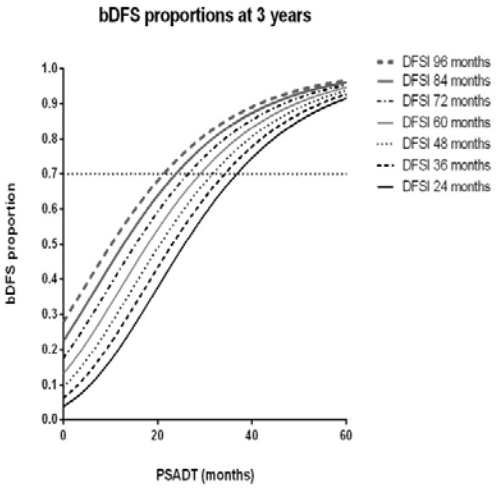
Purpose or Objective: Localized recurrent prostate cancer after primary radiotherapy can be curatively treated using salvage, including Iodine-125 brachytherapy (BT). Selection of patients for salvage is hampered by a lack of knowledge on predictive factors for cancer control, particularly in salvage BT. The aim of this study was to develop and internally validate a prediction model for biochemical failure (BF) after salvage I-125-BT using the largest cohort to date in order to aid patient selection in the future.

Material and Methods: Patients with a clinically localized prostate cancer recurrence who were treated with a whole-gland salvage I-125 implantation were retrospectively analyzed. Patients were treated in two centers in the Netherlands. Multivariable Cox-regression was performed to assess the predictive value of clinically relevant tumor-, patient- and biochemical parameters on BF, which was defined according to the Phoenix-definition (PSA-nadir+2 ng/ml). Missing data was handled by multiple imputation (20 datasets). The model's discriminatory ability was assessed with Harrell's C-statistic (concordance index). Internal validation was done using bootstrap resampling (using 2000 resampled datasets). Goodness-of-fit of the final model was evaluated by visual inspection of calibration plots, after which individual survival was calculated for categories of the predictor variables from multivariable analysis. All analyses were performed using the recently published TRIPOD statement.

Results: Sixty-two whole-gland salvage I-125-BT patients were identified. After median follow-up of 25 (range 0-120) months, 43 patients developed BF. In multivariable analysis, disease-free survival interval (DFSI) after primary therapy and pre-salvage prostate-specific antigen doubling time (PSADT) were predictors of BF; corrected hazard ratio (HR) 0.99 (95% confidence interval [CI]: 0.98-0.997 [p=0.01]) and 0.94 (95%CI: 0.90-0.99 [p=0.01]), respectively. Calibration plots demonstrated accurate predictive ability up to 36 months. The adjusted C-statistic was 0.71. Of patients with a PSADT>30 months and DFSI>60 months, >70% remained free of recurrence until 3 years. With every 12 months increase in DFSI, PSADT can decrease with 3 months to obtain the same survival proportion (Figure 1).



Conclusion: Salvage I-125-BT patients can be selected based on their disease free survival interval after primary therapy and the PSA-doubling time pre-salvage, ensuring sufficient biochemical control of >70% until three years.

OC-0065

Risk of second malignancies after seed prostate brachytherapy as monotherapy in a single institution

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Purpose or Objective: To report the incidence of second primary cancer (SPC) after Iodine-125 brachytherapy for early prostate cancer in a single institution with an intense urological surveillance and to compare it with the cancer incidence in the Australian population

Material and Methods: This retrospective, single-institution study included 889 patients treated with Iodine-125 brachytherapy alone. All the patients had a baseline cystoscopy before the implant. Data were collected on all subsequent SPC diagnoses. SPC incidences were retrieved for all type of cancers and for cancers close to the radiation field. Interval since the implant was evaluated for potential association to the treatment. Standardized incidence ratios (SIRs) were calculated for all cancers and for bladder cancers and matched with the general population. The absolute excess risk (AER) was expressed in relation to 10000 persons-years in the study. Kaplan-Meier analysis was used to determine the actuarial second malignancy and pelvic malignancy rates and the death from SPC and from any cause

Results: Patients were followed for a median of 4.16 (0-12) years with 370 (42 %) patients having 5 years or more follow up. 62 % patients were older than 60 years. 61 patients (6.8%) subsequently developed a SPC with 12 pelvic malignancies : 8 bladder and 4 rectal cancer. The 5- and 10- year cumulative incidences are 6.9% (95% Confidence Interval 5.0-9.4) and 19% (95% CI 14-26) for any second malignancy, 1.3% (95%CI 0.6-2.7) and 3.9% (95% CI 1.9-7.8) for any pelvic malignancy and 1% (95% CI 0.4-24) and 3.2% (1.4-7.1) for bladder cancer, respectively. The SIR was significantly higher for all pelvic malignancies at 2.10 (95% CI 1.09-3.67) and for all bladder cancers at 3.33 (95% CI 1.44-6.57). In the subgroup analysis bladder SPC risk was higher than expected for patients under 60 years (SIR 6.52; 95%CI 1.3-19; AER 13) and within the first 5 years of follow up (SIR 2.9 ; 95% CI 0.97-6.95; AER 10). Rectal cancer SIR were not significant or close in any of the categories. The 5- and 10-year rates of death from SPC were 1.9 % (95% CI 1.0-3.5) and 9.1% (95% CI 5.2-16) and from any cause were 3.2% (95% CI 2-5) and 14.4% (95% CI 9.5-21.6). On multivariable analysis, older age was associated with increased SPC risk (HR 1.05, p=0.021) , all cause mortality (HR 1.13, p<0.001) and mortality due to SPC (HR 1.09, p=0.014). Smoking status was associated with all cause mortality (HR 2.15, p=0.026) and with mortality from second malignancy (HR 2.59, p=0.045)

Conclusion: There may be an increased but small risk of second pelvic malignancy after prostate brachytherapy. A tendency towards a higher risk of bladder SPC after brachytherapy was found in the first 5 years of follow-up , probably resulting from screening bias . There was no significant increased rate of rectal cancer in any of the categories. Longer follow up is needed to draw strong conclusions.

OC-0066

Adaptive cone-beam CT planning improves progression-free survival for I-125 prostate brachytherapy

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Purpose or Objective: To determine the independent effect of additional intraoperative adaptive C-arm cone-beam computed tomography (CBCT) planning versus transrectal ultrasound (TRUS)-guided interactive planning alone in primary permanent I-125 brachytherapy for prostate cancer on long term biochemical disease free survival (bDFS).

Material and Methods: All patients with biopsy proven T1/T2-stage prostate cancer treated with I-125 brachytherapy were included in this cohort. Treatments were performed with TRUS-guided primary brachytherapy (+/- neoadjuvant hormonal therapy (NHT)) in a single institution in the period of November 2000 to December 2014. From October 2006 onwards, all patients received additional intraoperative adaptive CBCT planning for dosimetric evaluation and, if indicated, subsequent remedial seed placement in underdosed areas (which was performed in 15% of all patients). These procedures lasted 1-1.5 hours and were performed by a team of 2 radiation oncologists and 2 therapeutic radiographers. Pre-operative characteristics, follow-up PSA and mortality were prospectively registered. Patients were stratified into National Comprehensive Cancer Network (NCCN) risk groups. Kaplan-Meier analysis was used to estimate bDFS (primary outcome), overall survival (OS) and prostate cancer specific survival (PCSS) (secondary outcomes). Cox-proportional hazard regression was used to assess the independent predictive value of CBCT use on biochemical failure (BF) (Phoenix definition) and overall mortality (OM).

Results: 1623 patients were included. Median follow-up was 99 months (interquartile range (IQR) 70-115) for TRUS patients (n=613) and 51 months (IQR 29-70) for CBCT patients (n=1010). BF occurred 203 times and 206 patients died, of which 26 due to prostate cancer. For TRUS and CBCT patients, estimated 7-year bDFS was 87.2% vs. 93.5% (log rank: p=0.04) for low risk patients, 75.9% vs. 88.5% (p<0.001) for intermediate risk patients and 57.1 vs. 85.0% (p<0.001) for high risk patients. For TRUS and CBCT patients with low, intermediate and high risk disease, estimated 7-year OS was respectively 86.5% vs. 90.4% (p=0.11), 79.6% vs. 85.1% (p=0.30) and 66.4% vs. 84.2% (p=0.01). For TRUS and CBCT patients, 7-year PCSS was 96.0% vs. 100% (p<0.0001). After Cox regression, CBCT patients had lower rates of BF: HR 0.45 (95%-CI 0.33-0.61; p<0.0001). Corrected for age, IPSA, Gleason grade, T-stage, NHT-status and duration of NHT use, year of implantation, activity of the implant and prostate volume, CBCT showed to be an independent predictor of BF: HR 0.54 (95%-CI 0.33-0.89; p=0.02). CBCT was not an independent predictor of OM: HR 0.66 (95%-CI 0.40-1.07; p=0.09).

Conclusion: Additional intraoperative adaptive C-arm cone-beam CT planning in I-125 prostate brachytherapy leads to a significant increase in biochemical disease free survival in all NCCN risk groups.

Proffered Papers: Physics 1: Images and analyses

OC-0067

An automated patient-specific and quantitative approach for deformable image registration evaluation

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Purpose or Objective: In adaptive radiotherapy, deformable image registration (DIR) is used for contour propagation and dose warping. Contour evaluation is visual and qualitative and only accurate in high contrast regions. Dose warping requires fully spatial and quantitative DIR evaluation measures also valid in low contrast regions. While